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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,782	11/12/2003	Ping Jiang	312762004100	7794

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EXAMINER	
SANG, HONG	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 06/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/712,782	JIANG ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2 and 5-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RE: Jiang et al.

1. Applicant's response filed on 5/31/06 is acknowledged. Claims 1, 8 and 9 are amended. Claims 3 and 4 are cancelled. Claim 3 is amended. Claims 1-27 and 29-35 are pending. Claims 4-8, 17-24, and 30-35 are withdrawn.

2. Claims 1-3, 9-16, 25-27, and 29 are under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1, 2 and 5-11 are pending and under examination.

Rejections Withdrawn

5. The rejection of claim 9 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting the term "portions of said cells" is withdrawn in view of applicants' amendment to the claim.

6. The rejection of claims 1, 3, 4, 6, 7, 10 and 11 under 35 U.S.C. 102(b) as being anticipated by Hadjantonakis et al. (Histochem. Cell Biol. 2001, 115: 49-58) is withdrawn in view of applicants' amendment to the claim by reciting "microsurgically separating one or more living cells from a location in the tissue".

7. The rejection of claims 1-11 under 35 U.S.C. 103(a) as being unpatentable over Hadjantonakis et al. in view of Rashidi et al. (Clin. Exp. Metastasis 2000, 18: 57-60) is withdrawn in view of applicants' amendment to the claim by reciting "microsurgically separating one or more living cells from a location in the tissue".

New Grounds of Objections and Rejections

Claim Objections

8. Claim 1, 2 and 5-11 are objected to for reciting the phrase "separate from any cells that do not produce said first fluorescent protein" in claim 1 (see last line of claim 1). The recitation of this phrase is redundant (see line 4 of claim 1).

Claim Rejections - 35 USC § 112, 1st paragraph

9. Claims 1, 2, and 5-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **New Matter** rejection.

The term "from a location in the tissue" in claim 1 is considered new matter since the specification, and claims as filed disclose only "mechanically separating fluorescent tumor cells from surrounding normal tissue using the fluorescence emission as a guide" (see page 9, paragraph [0015], lines 3-5). There is no clear support for separating one or more living cells that produce a fluorescent protein "from a location in the tissue".

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

10. Claims 1, 2 and 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hadjantonakis et al. in view of Rashidi et al. (Clin. Exp. Metastasis 2000, 18: 57-60) and Trumper et al. (Blood, 1993, 81(11): 3097-3115).

Claims 1, 2 and 5-11 are drawn to a method to recover one or more fluorescent cells from a tissue, which method comprises microsurgically separating one or more living cells that produce a fluorescent protein in the tissue from any cells in the tissue that do not produce said first fluorescent protein, thereby recovering one or more living cells that produce said first fluorescent protein. Claims are further limited wherein cells that produce the first fluorescent proteins are tumor cells, the tumor cells are metastatic tumor cells of the lung, bone, lymph node or liver, the first fluorescent protein is a green fluorescent protein or a red fluorescent protein, said one or more living cells recovered consists of a single living cell, said cells that produce said first fluorescent protein are present in an immuno-compromised laboratory animal, the method further comprises transferring cells that produce said first fluorescent protein to at least one additional immuno-compromised animal, subjecting the recovered one or more living cells that produce said first fluorescent protein to gene expression analysis, said cells contained in the tissue that do not produce the first fluorescent protein produce a second fluorescent protein that emits a different wavelength from the first fluorescent protein.

Hadjantonakis et al. teach a method of isolating live GFP reporter-expressing cells from complex tissue by dissociation of the heterogeneous pool into single cells and subsequent flow sorting (page 56, Fig. 4). This involves the manual dissection cells and isolation of a region of interest harboring GFP positive cells, the subsequent enzymatic dissociation of the complex pool in order to produce individual cells, the live GFP positive cells are separated from live GFP negative cells by flow sorting (page 56, Fig. 4, and page 55, last paragraph). Hadjantonakis et al. teach that this methodology could

be applied to any tissue or organ of interest. Hadjantonakis et al. further teach a method of simultaneously isolating multiple different GFP reporter-expressing cells using mutually exclusive reporters e.g. yellow and cyan fluorescent reporters (see page 57, Figure 5 and 2nd paragraph, left column).

Hadjantonakis et al. do not teach that the GFP positive cells are microsugically separated from GFP negative cells. Hadjantonakis et al. do not teach that the cells that produce the first fluorescent protein are tumor cell, the tumor cells are metastatic tumor cells of the lung, bone, lymph node or liver, said cells that produce said first fluorescent protein are present in an immuno-compromised laboratory animal, transferring said cells to at least one additional immuno-compromised animal. However, these deficiencies are made up for in the teachings of Rashidi and Trumper.

Rashidi et al. teach that the Lewis lung carcinoma cells transduced with GFP gene can be transplanted to nude mice using surgical orthotopic implantation. The *in vivo* GFP-expressing tumors were then harvested and implanted as tissue fragments by surgical orthotopic implantation in the right lung of additional nude mice. This model resulted in rapid orthotopic growth and extensive metastasis visualized by GFP-expression.

Trumper et al. teach microsurgical separation of one or more desired cells based on cell surface staining and/or cell morphology (see Figure 1). The method comprises preparing viable single-cell suspensions from fresh tissue (lymph nodes) by mincing in RPMI 1640 medium and were either digested with collagenase or were pressed gently through a stainless steel mesh; identifying individual cells based on staining with certain

antibodies and/or morphology using phase-contrast microscope, and selecting the desired cells under inverted microscope with the help of a micromanipulator (see page 3096, last paragraph, page 3907, 1st paragraph and Figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Hadjantonakis to isolate living GFP expressing metastatic tumor cells by microsurgical separation instead of flow sorting and further transplant said tumor cells to an immunocompromised animals in view of the teaching of Trumper and Rashidi. One would have been motivated to modify the method of Hadjantonakis to isolate living GFP expressing metastatic tumor cells by microsurgical separation instead of flow sorting and further transplant said tumor cells to an immunocompromised animals because microsurgical separation method allows one to isolate desired cells based on cell staining and/or morphology when the expensive FACS machine is not available and it is as efficient as flow sorting when only small number of fluorescent cells are isolated, and Rashidi et al. teach that the use of GFP-transduced Lewis lung carcinoma transplanted by surgical orthotopic implantation is a very important useful model for metastasis, angiogenesis and therapeutic studies (see abstract, last sentence). Moreover, one of ordinary skill in the art would have a reasonable expectation of success to modify the method of Hadjantonakis to isolate living GFP expressing metastatic tumor cells by microsurgical separation instead of flow sorting and further transplant said tumor cells to an immunocompromised animals because Trumper teaches microsurgical separation of

cells and Rashidi et al. teach how to transplant the GFP expressing tumor cells from an immunocompromised animal to another immunocompromised animals.

Conclusion

11. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang
Art Unit 1643
June 13, 2005

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER